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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,859	09/20/2000	Marek Z. Kubin	1010-US	1889

7590 09/20/2002

Immunex Corporation
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EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	9

DATE MAILED: 09/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/667,859	KUBIN ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETIAL ACTION

Claims 73-89 are pending.

Response to the Amendment

This is a response to the amendment, paper No. 8, filed 07/17/2002. Claims 37-72 are canceled. Claims 73-89 are added and are considered.

Please note any ground of rejection that has not been repeated is removed.

The text of those sections of Title 35,US.Code not included in this section can be found in a prior office action.

Claim Rejections - 35 USC § 112

Claim 73-84 are a still rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73-84 are still vague and indefinite for using the open languages of " comprising" which fails to identify the precise claimed nucleic acid molecules as described in the previous office action.

Applicants argue that the term of "comprising" used in the rejected claims are as synonymous with " including" and containing or characterized by", which means the elements are essential, but other elements may be still form a structure within the scope of the claims.

Applicants' argument is respectfully; however, it is not found persuasive because the claims cannot define the precise structure of the claimed nucleic acid sequence, and the excluded elements are not taught or cannot be defined or described from the specification. If Applicants wish to claim a particular isolated nucleic acid molecule or protein/polypeptide, please amend the claim to a precise sequence structure of the intended molecule(s).

Claim Rejections - 35 USC § 112

Claims 73-89 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous office action, because the specification, while being enabling for an isolated nucleic acid molecule consisting of SEQ IN NO: 1 and its coding amino acid sequence

SEQ ID NO: 2, wherein its functional fusion proteins are made by its amino acid residues 1-221 with tags (SEQ ID Nos: 6-8), does not reasonably provide enablement for having any or all polynucleotide or amino acids fragment thereof having 80% homology to SEQ ID NO: 1 or 2 to be a functional molecule like NAIL. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants asserted that specification or the method in the art teaches how to make and use nucleic acid molecule encoding additional NAIL polypeptides because the cDNA (SEQ ID NO: 1) and amino acid sequence SEQ ID NO: 2 are provided, it is straight forward to determine what variations of these nucleotide and amino acid sequences falls within the 80% sequence identity limitation recited in the claims.

Applicants' argument has been fully considered; however, it is not found persuasive because one amino acid mutation in a sequence can turn the molecule to be a functional different one, i.e. the amino acid sequence of human chemokines, such as MIP-2α, MIP-2β and human GRO/MGSA as disclosed by Robin et al. (The cytokine Factors Book, Academic Press 1994, pp. 189) though they exhibit high homologies each from other (87%), but they function differently as described in the previous office action. Struffy et al demonstrate that a human chemokine RANTES lacking two N-terminal residue (3-68) lost its chemotactic activity significantly in monocyte and eosinophile in comparison with the full length non-truncated RANTES (Fig. 2 on page 1261).

In the instant case, Applicants only present use of a monoclonal antibody C1.7 to isolate claimed polypeptide SEQ ID NO: 2 and its extracellular domain fusion proteins of NAIL of SEQ ID NO: 6 and 8, which exhibit the NAIL function. Applicants do not present how to isolate any other polypeptide rather than SEQ ID NO: 6-8 having at least 80% homology to the SEQ ID NO: 2 that exhibits the same function of NAIL.

Because the claimed invention is directed to a structurally and functionally patentable distinct molecule, the precise molecular structure being able to exhibit the corresponding and the identical function should be disclosed.

Considering the broad scope of the claimed invention, it is still concluded that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 112

Claims 73-89 are still rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed any or all polypeptide having at least 80% or 90% homology to the SEQ ID NO:2.

Applicants submitted that the examiner has incorrectly applied the facts of Eli Illy Co. because the instant claims are drawn to the specific sequences described in the specification and any modifications of those specific sequences, which fall within the 80% or 90% sequence identity and still retain the ability to bind to CD48. Applicants maintains that by having possession of specific SEQ ID NO: 1 and 2, and by describing ways of various these specific sequences and tests for binding to CD48 in such detail as to enable those skill in the art, Applicants have fulfilled the written description requirement.

Applicants' argument has been respectfully considered; however it is not found persuasive because what do Applicants claim are any or all sequences having at least 80% homology of SEQ ID NO: 1 and 2.

In the instant disclosure, the applicants have only disclosed the sequences identified as NK cell activation inducing ligand (NAIL) encoded by nucleic acid sequence SEQ ID NO: 1, and amino acid sequence SEQ ID NO: 2 as well as the functional soluble extrcellular domain of amino acid residues (1-221) of SEQ ID Nos: 6, 7 and 8. However, no other sequences, which having at lease 80% homology to SEQ ID NO: 2 or fragment thereof exhibiting the same function like NAIL is disclosed. The situation would be the same to the Eli Lilly Co. because some sequence generated from a host, rather than human, may accidentally have 80% homology to the SEQ ID NO: 1 or 2. The applicant does not have the possession of any other molecules having at least 80% or 90% homology to the SEQ ID NO: 2, but rather than SEQ ID NO: 6-8,

which Applicants have possess and shown to exhibit the same function as peptide NAIL of SEQ ID NO. 2. Therefore, the claims 73-89 are still rejected under the 35 U.S.C. 112 1st paragraph.

Claim Rejections - 35 USC § 102

Claim 79 is still rejected under 35 U.S.C. 102(b) as being anticipated by Porunellor et al. (J. Immunol. 1993, Vol. 151, pp. 5328-5337).

Applicants argue that the mu2B4 disclosed by Porunelloor et al has only a 69% identity to the huNAIL as claimed in the present application, therefore, the claimed invention is not anticipated by the Porunellor et al.

Applicants'arguemnt has been fully considered; however, it is not found persuasive because the claimed product in the claim 79 is not only directed to the molecule having at least 80% homology to SEQ ID NO : 2, but also include other fragment thereof binding to CD48, which does not exclude the fragment disclosed by Porunellor et al. Therefore, the claimed invention is anticipated by the cited reference and the rejection is maintained.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

Claim 79 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter.which applicant regards as the invention.

Claim 79 is indefinite in that the metes and bonds of "fragment thereof" are not defined. The claim is interpreted in light of specification; however, the limitation of the specification cannot be read into claim. Therefore, the claim is considered indefinite.

Claim Rejections - 35 USC § 103

Claims 73-89 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Valiante et al. (US Patent No. 5,688,690A), Sambrook et al. (Molecular Cloning A laboratory

Manual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pp. 2.43-2.84) and Porunellor et al. (J. Immunol. 1993, Vol. 151, pp. 5328-5337) under the same ground as stated in the previous office action.

Claimed invention is drawn to an isolated polynucleotide encoded by the SEQ ID NO: 1 and its encoding amino acid sequence encoded by the SEQ ID NO: 2. The clone encoded by the SEQ ID NO: 1 is isolated by using a monoclonal antibody C1.7 (ATCC HB 117170) to screen a cell lines transfected with a human cDNA library prepared from the cytokine stimulated human NK cells, such as IL-2, IL-12, IL-15, INF-γ and anti-CD16. The cDNA encoding a p38 kD protein recognized by the monoclonal antibody C1.7 is isolated and sequenced. The extracellular domain of the said polynucleotide (1-221 amino acid residues) and its full length molecule have been tested to be able to bind the CD48 molecule and exhibit a co-stimulatory function in combining with the IL-4 and GM-CMS to activate the B cell and PBMCs.

Valiante et al. disclose that a novel monoclonal antibody (Amb) C1.7 (ATCC HB 117170) is able to recognize an antigen or cellular receptor, which recognize 38 kD protein, named P38. P38 is expressed in a NK cell and other CD8+ T cell upon activation by cytokines, such as IL2. Valiente also disclose all the function of p38, For example, the activation of p38 by C1.7 on CD8+ T cell mediates a non-MHC-restricted cytotoxicity; stimulates the lymphocyte proliferation, lymphokine production, signal transduction of NK cells and BLT-Esterase release from NK cells (Please see examples 4-10). Valiente et al. also teach several potential utilities for the novel protein p38, such as the use of identifying other ligands, the soluble p38, is possible, may be employed therapeutically to block ligands to CD8 cell to inhibit the CD8 T cell killing of target cells in the situation of a transplantation rejection or autoimmune destruction. The p38 also can be use for stimulating the immune response etc. (see the utilities of p38 disclosed in lines 8 on col. 8 through line 67 on col. 9). Valiente et al. do not disclose the sequence of the protein recognized by Amb C1.7. However, they stated in the Patent that the DNA and protein sequence of p38 can be obtained by resort to conventional methodologies known to one of skill in the art in view of the detail methods taught by Sambrook et al. (Molecular cloning A Laboratory Manual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pp. 2.43-2.84). Valianet et al. also explicitly teach the working examples (lines 48 on col. 7 through line 7 on col. 8 and examples 12 on col. 18 through 19) for isolating the cDNA clone encoding the protein p38 by

using Amb C1.7 to screen the protein expression in the cell transfected with the cDNA library and clone the corresponding cDNA into a plasmid to do the sequence analysis.

Porunellor et al. disclose a method that using cDNA library to do the molecule cloning the signal transducer molecule 2B4. They also disclose the sequence of the molecule having a high homology to the claimed molecule NAIL SEQ ID NO: 1, In addition they teach that this molecule can be expressed and purified by transfecting a mammalian cell.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Valiante et al. and combine the methods taught by et Valiante et al. Sambrook et al. and Porunellor et al. to either use the monoclonal antibody or cDNA to isolate the protein corresponding to the protein having the function of activating NK cell through binding the molecule of CD48. Hence, the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
September 17, 2002

ALI R. SALIMI
PRIMARY EXAMINER